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Low Proportion of Recent Human Immunodeficiency Virus (HIV) Infections among Newly Diagnosed Cases of HIV Infection as Shown by the Presence of HIV-Specific Antibodies of Low Avidity

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The time between human immunodeficiency virus (HIV) infection and diagnosis is mostly unknown. Two hundred five newly diagnosed patients were investigated for the duration of their HIV infection by avidity testing. Recent HIV infection was identified in 27.3% of the cases. Early diagnosis was achieved significantly less frequently in heterosexually infected persons than in other patients.

The diagnosis of a human immunodeficiency virus (HIV) infection is often delayed for years after the infection event (8). Knowing the infection time point would, however, be important for epidemiological surveillance, partner notification, or judging the likelihood of eventually detecting transmitted drug-resistant HIV strains (3, 4, 6).

Recently, on the basis of the knowledge that antibody avidity increases with time after infection (2), Suligoi et al. have reported that discrimination between HIV infections detected within 6 months of seroconversion and older infections is possible when the avidity of the virus-specific antibodies identified is determined (9). Similar data have been shown for various other viral infections before (1, 5, 7).

The aim of the present study was to assess the proportion of recent HIV infections among those routinely diagnosed in a population in which information about HIV transmission, diagnostic facilities, and antiretroviral treatment is widely available. For this purpose, an avidity test was established as previously described (9). As controls for recent infection, we included 12 serum samples obtained from 12 patients either within 3 months after the infection event, as indicated by the patients and confirmed by a negative HIV antibody test result prior to this event, or within 3 months after laboratory-proven seroconversion. As controls for long-term infection, 23 serum samples from patients infected with HIV for more than 1 year were analyzed. The data obtained are shown in Fig. 1. The difference between the mean avidity index (AI) of the recent infection controls (0.4085 ± 0.03709) and that of the long-term infection controls (0.9664 ± 0.01749) was statistically highly significant ($P < 0.0001$, unpaired t test). From our data, an AI of 0.8, selected as the border between low and high avidity, allowed complete discrimination between long-term infection and infection or seroconversion within 3 months before diagnosis. A previous study showed that an AI of <0.8 also exhibits high sensitivity and specificity for recent infections diagnosed within 6 months of seroconversion (10). Thus, in the further analysis we have considered an AI of <0.8 as being significantly associated with infection within the last 6 months.

It was then assessed how frequently HIV infection is already diagnosed in the Austrian population within the first months after infection. Between January 2002 and October 2003, 794 new HIV infections were diagnosed in Austria. Each case was serologically confirmed by enzyme-linked immunosorbent assay and Western blotting with two independent serum samples. For 205 (25.8%) of the patients, the serum sample used for the first diagnosis of HIV infection by antibody testing was still available. These samples had been obtained at various Aus-

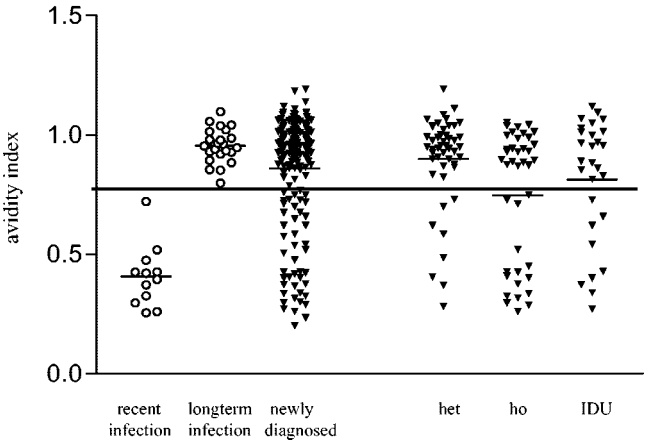

FIG. 1. HIV antibody AIs assessed with serum samples from 12 patients with recent HIV infections, from 23 long-term-infected patients, and from 205 patients newly diagnosed as HIV positive in 2002 and 2003 in Austria. In addition, the AIs associated with the individual infection risk groups of these newly infected patients are shown in detail. het, serum samples from 48 heterosexually infected patients; ho, serum samples from 40 homosexually infected patients; IDU, serum samples from 28 persons infected by IDU.

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TABLE 1. Association among early diagnosis of HIV infection (AI of <0.8), age, and gender

Group of patients with an AI of <0.8	No. of patients/total (%) whose age (yr) was:				
	<20	20–30	30–40	40–50	>50
Females	4/10 (40)	2/21 (9.5)	4/19 (21.1)	2/9 (22.2)	
Males	0/2	14/47 (29.8)	15/48 (31.3)	6/21 (28.6)	5/16 (31.3)
All	4/12 (33.3)	16/68 (23.5)	19/67 (28.4)	8/30 (26.7)	5/16 (31.3)

trian hospitals with the patients' informed consent. Samples were coded and further analyzed for the HIV antibody AI to assess retrospectively the interval between the infection event and the first diagnosis. The results obtained from the patients are shown in Fig. 1. In 56 (27.3%) of 205 patients, an AI of <0.8 was observed at the time of the first diagnosis of HIV infection. Thus, it was shown for the first time, to our knowledge, that even in a population in which information about HIV infection is widely distributed and to which diagnostic facilities are easily accessible, only about a quarter of the infections are detected within about 6 months after the infection event.

It was further investigated whether there was a connection between the time an HIV infection was diagnosed and the patient's gender or age. The patient group included 63 women (30.7%) and 142 men (69.3%). In 13 (20.6%) of the 63 female patients and 43 (30.3%) of the 142 male patients, an AI of <0.8 was identified at the first diagnosis. Although the women, in general, less frequently received an early diagnosis of HIV infection, the difference was not significant ($P > 0.176$, Fisher's exact test). The ages of 193 of the patients were known, and they ranged between 16 and 69 years. The results obtained with respect to age and gender are presented in Table 1. No significant association among age, gender, and early diagnosis of HIV infection was observed.

Finally, the association between early diagnosis of HIV infection and the route of transmission was also investigated. For 116 patients, the way they were infected was known; 48 were infected by heterosexual transmission, 40 were infected by homosexual transmission, and 28 were infected by intravenous drug abuse (IDU). The AIs of the individual risk groups are shown in Fig. 1, and the frequency of early HIV diagnosis is presented in Table 2. In the group of heterosexually infected persons, early diagnosis of HIV infection was achieved less frequently than in the other groups. The difference between early diagnosis of heterosexually versus homosexually transmitted infections was statistically significant ($P = 0.0175$, Fisher's exact test), as was the difference between these two groups when regarding only the male patients ($P = 0.0465$). These data indicate that heterosexually infected persons are less frequently undergoing early diagnosis of HIV infection. This may be due to different factors. On the one hand, the awareness of the heterosexual population of their infection risk is obviously especially low. On the other hand, the present findings may also mean that physicians confronted with the symptoms of acute HIV infection, which occur in about half of the primary infections (8), less frequently initiate further HIV-specific testing of heterosexual persons. This is probably due to the fact that HIV infections are still associated with certain risk groups. Recently, differences in achieving early diagnosis of HIV infection in nonwhite compared to white persons were described (11), also indicating that prejudgments of physicians are an important factor influencing the likelihood of achieving early diagnosis of HIV infection.

TABLE 2. Association between early diagnosis of HIV infection and mode of transmission

Group of patients with an AI of <0.8	No. of patients/total (%) whose mode of transmission was:			
	Heterosexual	Homosexual	IDU	Unknown
Females	5/27 (18.5)		3/9 (33.3)	5/27 (18.5)
Males	3/21 (14.3)	16/40 (40)	6/19 (31.6)	18/62 (29)
All	8/48 (16.7)	16/40 (40)	9/28 (32.1)	23/89 (25.8)

No significant differences were found in the detection of recent infections in persons infected by IDU versus heterosexually ($P = 0.155$, Fisher's exact) or homosexually ($P = 0.612$) infected persons, respectively.

In conclusion, our data show that about 70% of HIV infections in general and even more than 80% of heterosexually acquired HIV infections were detected more than 6 months after infection, providing prolonged opportunities for further HIV transmission. These findings demonstrate that even in a population in which information about HIV is widely distributed, awareness of the personal infection risk is still very low and is especially low in heterosexually infected persons.

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